

TOBACCO INDUSTRY RESEARCH COMMITTEE

350 FIFTH AVENUE NEW YORK 1, N. Y.

6. Budget Plan
 Includes CASI and Group Insurance
 full time employees

Salaries (Two Technicians)

Expendable Supplies

Application: For Research Grant

Overhead (12.5%)

Other

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* \$ 7,872.00

2,400.00

425.00

874.00

500.00 (travel)

\$12,071.00

February 7, 1955

for support of two beds, if monies
 are available.

Date:

Total

7. Name of Investigator of Work

and Years

Leonard E. Meiselas M.D., M.S., F.A.C.P.

2. Title: and Staff Available

A) Asst. Attend. Physician, Dept. of Med., Maimonides Hosp., Bklyn Clinical
 Spec. Instructor in Medicine, State University of New York, College of Medicine

B) Institution: New York City

C) P & Address: Consultant, Maimonides Hospital, 4802 Tenth Avenue, Brooklyn 19, N.Y., State
 University of New York, College of Medicine at New York City, Brooklyn, New York

4. Project or Subject:

1. To determine whether there is an abnormal steroid pattern in the tobacco patient compared with suitable controls.
2. To determine the metabolic pathways of compound E and Compound F in cancer patients, heart disease patients, tobacco users, and normal controls.
3. To determine whether Aldosterone is a normal or abnormal metabolic of E and F.
4. To determine whether the presence of an abnormal functioning liver is related to the production of Aldosterone.

9. Detailed Plan of Procedure (Use reverse side if additional space is needed); or sources of supply:

Dobriner has established that an abnormal steroid pattern can be demonstrated in the urine of some patients well in advance of the clinical detection of cancer. It has also been demonstrated that compound E and F may have ameliorating effects on the biology of certain tumors. Thus it appears certain that steroid metabolism is in some way intimately associated with the problem of neoplasia either causally or subsequently.

It has also been demonstrated that Aldosterone may be found in the urines of patients with congestive heart failure. No similar studies are available in the cancer patient. In addition, there is no information to our knowledge about the metabolic pathways of compounds E and F in the cancer patient, the heart disease patient, and the normal, with particular reference to the use of nicotine. In addition, the possibility that an abnormal steroid metabolism may exist has only been briefly studied. The possibility that Aldosterone may be part of an abnormal steroid response of the host either endogenously or in response to exogenous steroid has occupied our time and efforts for the past year. We have been able to set up successful analytical chromatography for the separations of compounds E and F, Tetrahydro E and Tetrahydro F. In addition, chromatographic systems for the separation of Aldosterone and Compound E have been developed. Bioassay studies in Adrenalectomized animals are in progress. Director of Project

Appropriate patients, reflecting the presence or absence of a positive tobacco history, presence or absence of cancer or heart disease will be admitted to the study beds of the Medical Services of the Maimonides Hospital of Brooklyn. Twenty-four hour urines will be collected, and plasma samples will be simultaneously prepared. Baseline excretions of compounds E and F, Tetrahydro E and F and 17 Ketosteroids

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will be determined by paper chromatography. Aldosterone will then be separated chromatographically from compound E and the final determination of the former will be done by bioassay of the eluate in the adrenalectomized rat against DCA standards.

Cortisone and Hydrocortisone will be administered orally in increasing doses to suitable patients. Urinary steroid excretions and simultaneous plasma levels of 17 Hydroxycorticoids will be done three times a week. Data will be collected to determine the amount of steroid excreted, excreted unchanged, or conjugated.

Blood and urinary sediments, chlorides and body weight will be determined daily. If and when edema occurs, urines will again be studied by paper chromatography for the presence of Aldosterone. If the latter is found, further studies on liver function will be performed by usual laboratory methods and by biopsy wherever possible.

The biochemical results in relation to metabolic pathways and abnormal steroid formation will be reviewed in the light of the patient's history with regard to smoking or non-smoking. The choice of patients will be made in such a fashion as to provide a suitable control series, e.g. males, females, smokers and non-smokers. It should be emphasized at this point that one of the patients that Debriner reported an abnormal steroid in advance of clinical cancer was a patient with carcinoma of the lung. This disease will be the first of the type of cancer that will be studied in the above protocol.

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6. Budget Plan:

*Includes OASI and Group Insurance
or full time employees

	Per Annum
Salaries (Two Technicians)	* \$ 7,872.00
Expendable Supplies	2,400.00
Permanent Equipment	425.00
Overhead (8.17%)	874.00
Other	500.00 (travel)
Total	\$12,071.00
Date	** \$7,300.00

** For support of two beds, if monies
are available.

7. Anticipated Duration of Work:

Two years

8. Facilities and Staff Available:

- A) Modern research laboratories, including chromatographic equipment, Beckman Spectrophotometer, Hood space, Centrifuge, and Flame photometer.
- B) Research Assistant with B.S., M.S.
- C) Research Consultant, Norman Weissman, Ph.D., Research Chemist to the Maimonides Hospital and Director of Chemistry Laboratories at Maimonides Hospital of Brooklyn.

9. Additional Requirements:

- One additional junior technician.
- Support for expendable supplies.
- Assumption of present assistant's salary.
- ** The support by grant of two beds would greatly facilitate admission of the necessary gross section of patients.

10. Additional Information (Including relation of work to other projects and other sources of supply):

This work has been supported completely by the Maimonides Hospital Research Funds for the past eighteen months. It has been demonstrated that compounds A and F may have some relationship to the biology of certain tumors. Thus it appears certain that steroid metabolism is in some way intimately associated with the problem of neoplasia either directly or indirectly.

It has also been demonstrated that Aldosterone may be found in the urine of patients with congestive heart failure. No similar studies are available in the cancer patients. In addition, there is no information in our knowledge about the metabolic pathways of compounds A and F in the cancer patient, the heart disease patient, and the normal, with particular reference to the use of Aldosterone. In addition, the possibility that abnormal steroid metabolism may exist has only been briefly studied. The possibility that Aldosterone may be part of an abnormal steroid response of the host either embryonically or in response to exogenous steroid has occupied our time and efforts for the past year. We have been able to set up

Approved

Dean, State University of New York, B. In addition, chromatographic systems for the College of Medicine at New York City. Compounds A and F have been developed. Aldosterone studies in neoplasia are in progress. Director of Project

Appropriate patients, reflecting the presence or absence of a positive tobacco history, presence or absence of cancer or heart disease will be admitted to the study. Urine of the Medical Services of the Maimonides Hospital of Brooklyn. Urine and plasma samples will be collected, and plasma Business Officer of the Institution prepared. Urine and plasma samples of compounds A and F, Testosterone 2 and F and 17 Ketotestosterone

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